Claims

1. A method for selecting, from a repertoire of polypeptides, a population of functional polypeptides which bind a target ligand in a first binding site and a generic ligand in a second binding site, which generic ligand is capable of binding functional members of the repertoire regardless of target ligand specificity, comprising the steps of-

a) contacting the repertoire with the generic ligand and selecting functional and polypeptides bound thereto; and

b) contacting the selected functional polypeptides with the target ligand and selecting a population of polypeptides which bind to the target ligand.

2. A method according to claim 1 wherein the repertoire of polypeptides is first contacted with the target ligand and then with the generic ligand.

3. A method according to claim 1 wherein the generic ligand binds a subset of the repertoire of polypeptides.

4. A method according to claim 3 wherein two or more subsets are selected from the repertoire of polypeptides.

5. A method according to claim 4 wherein the selection is performed with two or more generic ligands.

6. A method according to claims 4 or 5 wherein the two or more subsets are combined after selection to produce a further repertoire of polypeptides.

7. A method according to any preceding claim wherein two or more repertoires of polypeptides are contacted with generic ligands and the subsets of polypeptides thereby obtained are then combined.

8. A method according to any preceding claim, wherein the polypeptides of the repertoire are of the inimunoglobulin superfamily.

9. A method according to claim 8, wherein the polypeptides are antibody or T-cell receptor polypeptides.

10. A method according to claim 9, wherein the polypeptides are VH or VP domains.

11. A method according to claim 9, wherein the polypeptides are VL or Va domains.

12. A method wherein a repertoire of polypeptides according to claim 10 and a repertoire of polypeptides according to claim 1 are contacted with generic ligands and the subsets thereby obtained are then combined.

13. A method according to any preceding claim wherein the generic ligand is selected from the group consisting of a matrix of metallic ions, an organic compound, a protein, a peptide, a monoclonal antibody, a polyclonal antibody population, and a superantigen.

14. A method for detecting, inimobilising, purifying or inimunoprecipitating one or more members of a repertoire of polypeptides previously selected according to any one of claims 1 to 13, comprising binding the members to the generic ligand.

15. A library wherein the functional members have binding sites for both generic and target ligands.

16. A library designed for selection with both generic and target ligands.

17. A library according to claim 15 and 16 comprising a repertoire of polypeptides of the inununoglobulin superfamily.

18. A library according to claim 17 wherein the polypeptides are antibody or T-cell receptor

polypeptides.

19. A library according to claim 18, wherein the polypeptides are VH or VP domains.

20. A library according to claim 18, wherein the polypeptides are VL or Vcc domains.

21. A library wherein a repertoire of polypeptides according to claim 19 and a repertoire of polypeptides according to claim 20 are contacted with generic ligands and 0 the subsets thereby obtained are then pooled.

22. A library according to any one of claims 15 to 21, wherein the functional members of the repertoire have a known main-chain conformation.

23. A library according to claim 22, wherein the functional members of the repertoire have a single main-chain conformation.

24. A library according to claims 22 or 23, wherein the immunoglobulin scaffold is based on gerniline V gene segment sequences.

25. A library according to any one of claims 15 to 24, wherein the polypeptides are varied at random positions.

26. A library according to any one of claims 15 to 24, wherein the polypeptides are varied at selected positions.

27. A library according to claim 26, wherein the selected positions are those which form the binding site for the target ligand.

28. A library according to claim 27, wherein the selected positions are a subset of those which form the binding site for the target ligand.

29. A library wherein a repertoire of polypeptides according to claim 28 is first contacted with a target ligand in order to isolate a subset of polypeptides specific for the target ligand, the subset

of polypeptides then being varied at a further subset of residues in order to modify the function, specificity or affinity of target ligand interaction.

30. A library according to claims 26-29, wherein the variation is achieved by incorporating all 20 different amino acids at the positions to be varied.

31. A library according to claim 26-29, wherein the variation is achieved by incorporating some but not all of the 20 different amino acids at the positions to be varied

32. A nucleic acid library encoding a library of polypeptides according to any one of claims 15 to 31.

add

C7